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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/944,396	08/30/2001	Kevin P. Baker	P2548P1C11	2338

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EXAMINER	
KEMMERER, ELIZABETH	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 11/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/944,396	BAKER ET AL.	
	Examiner	**Art Unit**	
	Elizabeth C. Kemmerer, Ph.D.	1646	

--The MAILING DATE of this communication appears on the cover she t with the correspondence address --

THE REPLY FILED 16 June 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on *14 August 2003*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *please see attachment*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *22-26*.

   Claim(s) withdrawn from consideration: _____.

8. ☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

ATTACHMENT TO ADVISORY ACTION

1) Claims 22-26 remain rejected under 35 U.S.C. §§101 and 112, first paragraph, for reasons of record.

Applicant's arguments (response received 16 June 2003) have been fully considered but are not found to be persuasive for the following reasons. Applicant refers to publications submitted as an attachment as providing evidence that mRNA levels correlate with protein levels. Therefore, Applicant concludes that one skilled in the art would reasonably expect that the specification's disclosure of data regarding altered mRNA levels in certain cancer types extend to altered protein levels, thus providing a credible, specific and substantial utility for the claimed antibodies. This has been fully considered but is not found to b persuasive. Each publication will be addressed in turn.

Maruyama et al. (1999, Am. J. Path. 155:815-822) show that Id-1, Id-2 and Id-3 mRNAs are overexpressed in pancreatic cancer cells (p. 818, middle of right column); however, only Id-1 and Id-2 protein levels were clearly expressed at higher levels in pancreatic cancer cells as compared to normal pancreatic cells (p. 819, right column). See also, p. 821, left hand column: "Id-3 mRNA levels did not correlate well with Id-3 protein expression."

Ginestier et al. (2002, Am. J. Path. 161:1223-1233) show that two thirds of the tested molecules showed **no correlation** between the cDNA (mRNA-based assay) and tissue array (protein-based assay) analyses. See abstract.

Dalifard et al. (1998, Int. J. Mol. Med. 1:855-861) show a good correlation between DNA amplification and protein overexpression for c-erbB-2 in breast cancer.

Hareuveni et al. (1990, Eur. J. Biochem. 189 :475-486) show that RNA and protein are overexpressed from the VNTR gene in breast cancer.

Barr et al. (2003, J. Parasitol. 89 :381-384) disclose data relevant to Chagas disease, an infectious (non-cancerous) disease. This reference is not found to be relevant.

When the evidence is viewed as a whole, we see that the specification provides data that the nucleic acid of SEQ ID NO: 68 is elevated in certain cancers, providing a specific, substantial and credible utility for the nucleic acid. However, the instant claims are to antibodies. This utility would only extend to the antibodies if it can be established that the elevation of nucleic acid in cancer is predictive of the overexpression of the encoded protein in the same cancer. The secondary evidence does not support this. Dalifard et al. and Hareveni et al. support Applicant's position by demonstrating a good correlation for 2 examples. However, Maruyama et al., Ginestier et al. and the references cited by the examiner in the previous Office Action show more examples wherein the elevated nucleic acid levels are not predictive of elevated protein levels. Thus, the evidence as a whole indicates that the rejections are appropriate.

If Applicant is aware of any post-filing date data regarding the overexpression of the protein of SEQ ID NO: 69 in cancerous tissue sample, such would be considered probative.

2) Claim 22 remains rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for reasons of record.

Applicant argues that one skilled in the art would recognize the definition of "specifically binds". This has been fully considered but is not found to be persuasive because "specifically" is a relevant term. Neither the art nor the specification provides an unambiguous definition of the term, such that the metes and bounds of the claimed antibodies cannot be determined.

3) The effective priority date for the instant application remains determined to be 30 August 2001. Applicant's arguments have been fully considered but are not found to be persuasive, since the utility and enablement rejections have been maintained as explained above.

4) Claims 22-26 remain rejected under 35 U.S.C. § 102 (a) and (e) as being anticipated by U.S. Patent 6225085.

Applicant's arguments have been fully considered but are not found to be persuasive for the following reasons. Applicant argues that SEQ ID NO: 69 recited in the claims is not identical to the sequence disclosed in the reference, and thus the reference does not anticipate the claims. this has been fully considered but is not found to be persuasive because an antibody doesn't recognize the whole protein, just an antigenic site. Since the protein recited in the claims and in the prior art are identical in

598 out of 673 amino acids, it is clear that most antibodies would cross-react with both proteins. The antibody is being claimed, not the protein.

Applicant also refers to Bowie et al. and Chaudhuri et al. as evidence supporting the argument that minor changes in sequence can greatly alter antigenic sites. Applicant concludes that one cannot assume that the protein recited in the claims and the protein of the prior art would present the same antigenic sites. This has been fully considered but is not found to be persuasive. This reasoning may be true for some antibodies that recognize composite, or conformational, antigenic sites, but it would not be true for antibodies that recognize linear antigenic sites. The prior art is not limited to composite, or conformational, antibodies. In fact, the prior art specifically suggests using (linear) fragments to generate antibodies. These would be expected to cross-react.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth C. Kemmerer, Ph.D. whose telephone number is (703) 308-2673. The examiner can normally be reached on Monday through Thursday, 7:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne L. Eyler, Ph.D. can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Elizabeth C. Kemmerer

ECK

ELIZABETH KEMMERER
PRIMARY EXAMINER